REMARKS

Claims 7, 9, 12, 13, 18, 20, 23, 26 and 27 are in the case. Claims 1-6, 8, 10-11, 14-17, 19, 21-22 and 24-25 were cancelled and claims 26-27 are new. Claims 7, 9, 12, 13, 18, 20 and 23 have been amended in view of the Office Action and to better define what the Applicants consider their invention.

Reconsideration in view of the following remarks and entry of the foregoing amendments are respectfully requested.

SEQUENCE COMPLIANCE

The Examiner requested that the brief description of Figure 7A be amended to include a reference to SEQ ID NO: 6.

The disclosure was amended accordingly.

SPECIFICATION

The specification was amended to correct the typographical error, remove the hyperlink and update the status of USSN 09/785,301 as suggested by the Examiner.

DRAWINGS

The Examiner requested that a description of element F of Figure 1 be provided in the description or removed from the Figure 1.

The description was amended accordingly. Support for the amendment may be found in Figure 4a.

CLAIMS OBJECTIONS

Claims 8-13 and 19-23 are objected to because they refer to "a" method of a previous claim instead of "the" method of the previous claim.

Claims 8, 10-11 and 21-22 are cancelled. Claims 9, 12-13, 20 and 23 were amended accordingly and new claims 26-27 correctly recite "the" method.

Claims 7-13 and 18-23 are objected to because they depend from withdrawn claims.

Claims 8, 10-11, 21-22 were cancelled and claims 7, 9, 12-13, 18, 20 and 23 were amended accordingly and new claims 26-27 depend from pending claims.

DOUBLE PATENTING

Claims 7-13 and 18-23 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 31-39 and 44 of copending Application No. 10/530,413.

The Applicants duly note this provisional rejection but do not wish to address it at this time. The Applicants recognize that this objection may continue to be made by the Examiner in this application as long as she is of opinion that there are conflicting claims in the two applications that are the subject of this rejection, subject to the following: "[I]f this "provisional" non statutory obviousness-type double patenting (ODP) rejection is the only rejection remaining in the earlier filed of the two pending applications, while the later is rejectable on other grounds, the Examiner should withdraw that rejection and permit the earlier filed application to issue as a patent without a terminal disclaimer" (MPEP 804 I.B.1).

The present application is the earlier filed of the two applications that are the subject of the present rejection. Indeed, the parent application 09/785,301 now abandoned of the instant application was filed on February 20, 2001 while the PCT application from which '413 constitutes a national phase was filed on October 6, 2003. The Applicant therefore does

not wish to address this issue in the present response since the provisional rejection may be withdrawn.

REJECTIONS UNDER 35 U.S.C. § 112 SECOND PARAGRAPH

The Examiner has rejected claims 10, 11 (and dependent claims 12-13), 21 and 22 under 35 U.S.C. § 112, second paragraph as being indefinite in their recitation of a "HIV-derived peptide".

This rejection is rendered moot by the cancellation of claims 10, 11, 21 and 22.

The Examiner has rejected claims 13 and 23 under 35 U.S.C. § 112, second paragraph as being indefinite in their recitation "wherein said hematopoietic stem cell is human ".

Claims 13 and 23 were amended accordingly.

In view of the above and foregoing, it is respectfully requested that the Examiner withdraw her rejection of claims 10, 11 (and dependent claims 12-13), 21 and 22 under 35 U.S.C. § 112, second paragraph.

REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 7, 9-13, 18 and 20-22 have been rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description and enablement requirement. The Applicants respectfully traverse the rejection as follows.

With regards in particular to the rejection on the basis of written description, the Examiner states that "the rejected claims thus comprise a genus of proteins that are defined by function: (1) have the enhancement activity of a hox peptide, and (2) are capable of crossing the cell membrane."

As indicated above, claims 10-11 and 21-22 are now cancelled. Although the Applicant disagrees with the Examiner's assessment, in order to accelerate allowance, Claims 7, 9-13, 18 and 20-22 and new claims 26-27 recite a stem cell expansion factor which comprises a HOXB4 protein and a NH_2-terminal protein transduction domain (PTD) from a transactivating protein (TAT).

With regards in particular to the rejection on the basis of enablement, the Examiner states that "while being enabling for a method for enhancing expansion of a stem cell population, the method comprising directly delivering to a stem cell population an effective amount of a HOXB4 protein conjugated to an HIV transactivating protein (TAT) protein transduction domain, does not reasonably provide enablement for fragments of any hox protein or full-length proteins not taught as having stem cell expansion activity".

Although the Applicant disagrees with the Examiner's assessment, in order to accelerate allowance, claims 7, 12-13, 18 and 20 have been amended to cover only subject matter deemed enabled by the Examiner. Claims 9-11 and 21-22 were cancelled.

In view of the above and foregoing, it is respectfully requested that the Examiner withdraw her rejection of claims 7, 9-13, 18 and 20-22 under 35 U.S.C. § 112, first paragraph.

REJECTION UNDER 35 U.S.C. § 103

Claims 7-13 and 18-23 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Largman et al in view of Frankel et al.

In Largman et al., stem cells were modified by the incorporation of exogenous genetic material into their genome. The introduction of the exogenous genetic material is preferentially performed by retroviral infection. The modified stem cell overexpressing HOXB4 is characterized by an enhanced ability to undergo self-renewal as compared to unmodified stem cell.

Franckel *et al.* teach the delivery of biologically active proteins to the cytoplasm

and nuclei by the use of transport polypeptides which comprise a HIV tat protein covalently attached to the cargo.

Applicants respectfully traverse the rejection as follows.

Failures of others

It is first submitted that failures are rarely reported in the literature and Applicant is thus not aware of a publication reporting a failed attempt to achieve a functional TAT-HOXB4. However, none of the more than 50 laboratories which received HOXB4 cDNA constructs from the inventors following their paper of 1994 reported success with a non-gene transfer of HOXB4 while drawbacks of gene transfer were known. The Examiner is referred to Keith Humphries' Declaration under CFR 1.132 in support of these allegations.

Unpredictability

It is not routine experimentation to produce a functional stem cell expansion factor which comprises a HOXB4 protein and a NH_2-terminal protein transduction domain (PTD) from a transactivating protein (TAT) and that it was not predictable whether functional Hoxb4 non-gene delivery could be achieved.

Hurdles to overcome in this research program included methods of production, purification and storage, dosage (amount and frequency); *in vitro* conditions, and nature of starting cells that would respond. It could not be predicted either whether the purified HOXB4 would keep its biological activity (transcriptional modifications, stability, etc.). The Examiner is referred to Keith Humphries' Declaration under CFR 1.132 in support of these allegations.

Long-felt but unresolved need

It is further submitted that there was a long-felt but unresolved need for the methods of the present invention. According to the World Health Organization, the number of patients having blood cancer in Europe and North America in need for HSCs transplantation was about 265,000 in 2007. Half of these patients die annually, the majority of them because they did not have access to a HSCs transplantation.

However, the prior art technique of delivering HOXB4 to stem cells, namely HOXB4 gene transfer, possesses significant disadvantages. Frankel disclosed certain disadvantages of gene delivery techniques. Another probably more challenging drawback of gene transfer is the risk of insertional mutagenesis leading to leukemia. The Examiner is referred to Denis-Claude Roy's Declaration under CFR 1.132 in support of these allegations.

Commercial success

At last, a declaration is submitted attesting of the commercial success of the present technology. Dr. Roy and other colleagues of Hôpital Maisonneuve-Rosemont have obtained a pre-IND visit to request approval of Health Canada to conduct clinical studies with the HOXB4 construct of the present invention. Health Canada's response was very positive and work is underway to satisfy the Government requirements. The Examiner is referred to a Declaration under CFR 1.132 by Dr. Denis-Claude Roy, who will be leading the clinical trials in support of these allegations.

The rejections of the original claims are believed to have been overcome by the present remarks and the introduction of new claims. From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order, and such an action is earnestly solicited.

PETITION FOR THREE-MONTH EXTENSION OF TIME

Applicants hereby request that the period for responding to the Office Action dated October 18, 2007, and originally set to expire January 18, 2008, be extended by three (3) months, so as to expire on April 18, 2008.

The Commissioner is authorized to charge the amount of $525, to cover the three-month extension herein requested, to Deposit Account No. 07-1742. The Commissioner is further authorized to charge any deficiencies or to credit any overcharges to this same Deposit Account number.

Favorable action on this request for extension of time is courteously solicited.

Authorization is hereby given to charge Deposit Account no. 07-1742 for any deficiencies or overages in connection with this response.

Respectfully submitted,

Date: April 17, 2008

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JG/cd
Encl. Keith Humphries' Declaration under 37 CFR 1.132; and
Denis-Claude Roy's Declaration under 37 CFR 1.132.